AMENDMENTS

Listing of Claims

The following listing of claims replaces all previous listings or versions thereof:

1. (Presently amended) A transgenic mouse, the cells of which comprise at least one endogenous altered LXRα allele, wherein said altered LXRα allele comprises the insertion of a selectable marker gene, ~~that cannot express LXRα that responds to dietary cholesterol~~, wherein said mouse shows a phenotype of increased hepatic cholesterol accumulation when fed a 2% cholesterol diet for seven days compared to a control animal.

2. (Presently amended) The transgenic mouse of claim 1, wherein said cells comprise two endogenous altered LXRα alleles, wherein said altered LXRα alleles both comprise the insertion of a selectable marker gene ~~that cannot express LXRα that responds to dietary cholesterol~~, and wherein said mouse shows a phenotype of hepatomegaly when fed a 2% cholesterol diet for ninety days.

3. (Canceled)

4. (Previously amended) The transgenic mouse of claim 1, wherein a transcript produced from said endogenous altered LXRα allele contains an interruption in the LXRα coding sequence.

5. (Previously amended) The transgenic mouse of claim 2, wherein a transcript produced from said endogenous altered LXRα alleles both contain an interruption in the LXRα coding sequences.

6. (Previously amended) The transgenic mouse of claim 1, wherein said endogenous altered LXRα allele contains a nonsense mutation that truncates the corresponding encoded LXRα polypeptide.

7. (Previously amended) The transgenic mouse of claim 2, wherein said endogenous altered LXRα alleles both contain a nonsense mutation that truncates the corresponding encoded LXRα polypeptide.

8. (Previously amended) The transgenic mouse of claim 1, wherein said endogenous altered LXRα allele contains a deletion of LXRα coding sequences.

9. (Previously amended) The transgenic mouse of claim 2, wherein said endogenous altered LXRα alleles both contain a deletion of LXRα coding sequences.

10. (Previously amended) The transgenic mouse of claim 1, wherein said endogenous altered LXRα allele contains a mutation in the 5' regulatory region of the LXRα gene.

11. (Previously amended) The transgenic mouse of claim 2, wherein said altered endogenous LXRα alleles both contain a mutation in the 5' regulatory region of the LXRα genes.

12. (Previously amended) The transgenic mouse of claim 10, wherein said alteration comprises substitution of an inducible/repressable promoter for the endogenous LXRα promoter.

13. (Previously amended) The transgenic mouse of claim 11, wherein said alterations comprise substitution of inducible/repressable promoters for both of the endogenous LXRα promoters.

14-20. (Canceled)

21. (Presently amended) A method for screening a candidate substance for the ability to reduce cholesterol levels via LXRα in a mammal comprising:

(a) providing a transgenic mouse, the cells of which comprise at least one endogenous altered LXRα allele, wherein said altered LXRα allele comprises the insertion of a selectable marker gene ~~that cannot express LXRα that responds to dietary cholesterol~~;

(b) treating said mouse with said candidate substance; and

(c) monitoring a cholesterol-related phenotype in said mouse,

wherein a reduction in said cholesterol-related phenotype in said mouse treated with said candidate substance, as compared to a similar mouse not treated with said candidate substance, indicates that said candidate substance reduces cholesterol levels via an LXRα-independent mechanism.

22. (Canceled)

23. (Original) The method of claim 21, wherein said phenotype is cholesterol absorption, circulating cholesterol, hepatic cholesterol, hepatomegaly, atherosclerosis, cardiac failure, cardiac (atrophy/hypertrophy), activity level, survival, cancer, reproduction, immune function, skin disease, cognitive function, and adrenal function.

24. (Previously amended) The method of claim 21, wherein said mouse is maintained on a high cholesterol diet.

25. (Previously amended) The method of claim 21, wherein said mouse further is treated with an agent that blocks cholesterol biosynthesis.

26. (Presently amended) The method of claim 21, wherein said cells comprise two endogenous altered LXRα alleles ~~that cannot express LXRα that responds to dietary cholesterol~~, each allele comprising the insertion of a selectable marker gene.

27. (Presently amended) A method for screening a candidate substance for the ability to increase bile acid synthesis via LXRα in a mammal comprising:

(a) providing a transgenic mouse, the cells of which comprise at least one endogenous altered LXRα allele, wherein said altered LXRα allele comprises the insertion of a selectable marker gene ~~that cannot express LXRα that responds to dietary cholesterol~~;

(b) treating said mouse with said candidate substance; and

(c) monitoring a bile acid-related phenotype in said mouse,

wherein an increase in said bile acid-related phenotype in said mouse treated with said candidate substance, as compared to a similar mouse not treated with said candidate substance, indicates that said candidate substance increases bile acid synthesis via an LXRα-independent mechanism.

28. (Canceled)

29. (Original) The method of claim 27, wherein said bile acid-related phenotype is selected from the group consisting of cholesterol level, Cyp7a synthesis, fecal bile acid excretion, bile acid pool size and bile acid composition.

30-43. (Canceled)

44. (Presently amended) A transgenic mouse cell which comprises at least one endogenous altered LXRα allele, wherein said altered LXRα allele comprises the insertion of a selectable marker gene ~~that cannot express LXRα that responds to dietary cholesterol~~.

45. (Presently amended) The transgenic cell of claim 44, wherein said cell comprises two endogenous altered LXRα alleles, wherein said altered LXRα alleles both comprise the

insertion of a selectable marker gene ~~that cannot express LXRα that responds to dietary cholesterol~~.

46-58. (Canceled)